Pharmacy and Therapeutics Committee Meeting Record

Date: 10/19/07 **Time:** 9:00 a.m. – 3:30 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Conference Room D

Moderator: Don Norris, M.D.

Committee Members Present: Phil Petersen, M.D.; Thomas Rau, M.D.; William Woodhouse, M.D.; Donald Norris, M.D.; Tami Eide, PharmD; Michelle Miles, PA-C; Rick Sutton, RPh; Rex Force, PharmD; Stan Eisele, M.D; Tim Rambur, PharmD; Mark Johnston, RPh; Catherine Gundlach, PharmD;

Others Present: Steve Liles, PharmD; Selma Gearhardt, PharmD; Kathy Eroschenko, PharmD; Bob Faller; Rachel Strutton

Committee Members Absent: Andrew Olnes, M.D.

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	Don Norris, M.D.	Dr. Norris called the meeting to order.
Committee Business		
➢ *Roll Call & Introduction of new P&T members Tim Rambur, PharmD and Mark Johnston, RPh*	Don Norris, M.D.	Dr. Rambur is a practicing pharmacist at an independent pharmacy in the Twin Falls area and Mr. Johnston is the new Executive Director for the Idaho Board of Pharmacy.
➢ *Reading of Confidentiality Statement*	Don Norris, M.D.	Dr. Norris read the Confidentiality Statement
➢ *Approval of Minutes from August 17, 2007 Meeting*	Don Norris, M.D.	There were no corrections. Minutes were approved as published.
➢ *DERP Updates*	Tami Eide, PharmD	Dr. Eide presented key questions for the following topics from the Drug Effectiveness Review Project: • Diabetes Drugs • Asthma • Opioids • Alzheimer Drugs • TZD Drugs

		Dr. Eide announced the completion of these final reports from the Drug Effectiveness Review Project • Constipation Drugs • Beta Blockers Update #3 • Neuropathic Pain Dr. Eide discussed these scans from the Drug Effectiveness Review Project • 2nd Generation Antidepressants – will update • NSAIDs- will not update • Beta Agonists-will change to beta agonists for rescue since asthma report is covering controller medication

Public Comment Period	Don Norris, M.D. Bob Faller, Medical Program Specialist	Twenty-three (23) people signed up to speak during the public comment period. Public comment was received from the following speakers:

Speaker	Representing	Agent	Class
Dr. J Anthony Lopez	Self	Coreg CR	Beta Blockers
Heather Cowden RN (Call in)	Self	Pegylated Interferons	Hepatitis C Agents
Tracy Young	Self	Pegylated Interferons	Hepatitis C Agents
Lynn Lundquist	Self	Detrol LA	Bladder Relaxants
Ellen Hunter, M.D. (Call in)	Self	Pegylated Interferons	Hepatitis C Agents
William Damarod, M.D. (Call in)	Self-Eagle Rock Neurology	Multiple Sclerosis Agents	Multiple Sclerosis Agents
William Schmidt	Penn Pharma	Avodart	BPH Agents
Don Moran	Sanofi Aventis/UCB Pharm	levocetirazine	Antihistamine, Minimally Sedating
Christopher Spell	Sanofi Aventis	Uroxatral	BPH Agents
Kyle Downy	Sanofi Aventis	Lovenox	Anticoagulants, Injectable
Molly Roy, PA	Self-Rocky Mountain Clinic	Multiple Sclerosis Agents	Multiple Sclerosis Agents
Rosalynde Finch	Biogen Idec	Avonex Tysabri	Multiple Sclerosis Agents

Long Nguyen	SmithKlineBeecham	Coreg CR	Beta Blocker
Heather Potter	National Multiple Sclerosis Society	Multiple Sclerosis Agents	Multiple Sclerosis Agents
Fred Amberger	Novartis	Enablex	Bladder Relaxants
Sylvia Foster	GlaxoSmithKline	Arixtra	Anticoagulants, Injectable
Leigh Platty	Astellas	VESIcare	Bladder Relaxants
Gina Guinasso	EMD Serono	Rebif	Multiple Sclerosis Agents
Robert Martin	Bayer	Betaseron	Multiple Sclerosis Agents
Sue Heineman	Pfizer	Detrol LA	Bladder Relaxants
Vandanna Slater	Roche	Pegasys	Hepatitis C Agents
Karina Kuznetsova	Schering-Plough	Peg-Intron	Hepatitis C Agents
Jack Kriegen	Boise Hepatitis C Group	Hepatitis C Agents	Hepatitis C Agents

Drug Class Review		
➢ Phosphate Binders	Steve Liles, PharmD	Phosphate Binders Dr. Liles stated the class was last reviewed May 2006. New evidence since our last review was presented. Mr. Liles reviewed the indications and reviewed three (3) clinical trials.
➢ Beta Blockers	Kim Peterson, MS OHSU EPC	Beta Blockers Ms. Peterson shared update #3 for a Drug Class review that was completed in September 2007. The major change for this update was the inclusion of carvedilol extended-release - Coreg CR.. Newer trials were evaluated for all agents. Overall there was no new evidence to change conclusions of previous reports..
➢ Hepatitis C Agents	Roger Chou, MD, OHSU EPC	Hepatitis C Agents Dr. Chou shared results from the Drug Class Review on pegylated interferons for chronic hepatitis C infections that was completed in May 2007. The EPC evaluation concluded that the overall quality of evidence was fair to poor and there was insufficient evidence to determine differences between the two pegylated products for efficacy or safety.
➢ Multiple Sclerosis Agents	Marian McDonagh, PharmD OHSU EPC	Multiple Sclerosis Agents Dr. McDonagh shared results from the Drug Class Review on disease-modifying drugs for multiple sclerosis that was completed in July 2007. The EPC compared the agents for safety and efficacy in relapsing, remitting Multiple Sclerosis, secondary progressive multiple sclerosis, primary progressive multiple sclerosis and progressive relapsing multiple sclerosis. The overall quality of evidence was fair to poor and results were mixed.

Committee Clinical Discussions and Conclusions	Don Norris, MD	Phosphate Binders No compelling clinical data to support any changes at this time. Hepatitis C Agents No compelling clinical data to support any changes at this time. Multiple Sclerosis Agents No compelling clinical data to support any changes at this time. Patient uniqueness supports having all agents available without restrictions. Beta Blockers No compelling clinical data to support any changes at this time.
Drug Class Reviews Continued		
➢ Anticoagulants, Injectables	Steve Liles, PharmD	Anticoagulants, Injectables Dr. Liles stated the class was last reviewed October 2006. He also shared the new indication for dalteparin, as well as the updated guidelines.
➢ Antihistamines, Minimally Sedating	Steve Liles, PharmD	Antihistamines, Minimally Sedating Dr. Liles stated the class was last reviewed July 2006. There is a new drug in this class levocetirizine (Xyzal). Dr. Liles reviewed the indications and the Pharmacokinetices of the new drug. Three (3) clinical trials were reviewed. Dr. Liles also shared the usage in special populations as well as the warnings and contraindications.
➢ Bladder Relaxants	Steve Liles, PharmD	Bladder Relaxants Dr. Liles stated the class was last reviewed October 2006. Dr. Liles shared one (1) clinical trial as well as one (1) systematic review. Also reviewed was a retrospective analysis for pediatrics.
➢ BPH Agents	Steve Liles, PharmD	BPH Agents Dr. Liles stated the class was last reviewed October 2006. Dr. Liles shared the indications with in this class. He also reviewed one (1) clinical trial and one (1) systematic review.
➢ Calcium Channel Blockers	Steve Liles, PharmD	Calcium Channel Blockers Dr. Liles stated the class was last reviewed October 2006. There are two (2) new generics in this class, Norvasc (amlodipine) and Verelan PM (verapamil CR). Dr. Liles reviewed one (1) clinical trial as well as updated pulmonary artery hypertension guidelines.

Committee Clinical Discussions and Conclusions continued	Don Norris, MD	Anticoagulants, Injectables No compelling clinical data to support any changes at this time. Antihistamines, Minimally Sedating No compelling clinical data to support any changes at this time. Bladder Relaxants No compelling clinical data to support any changes at this time. BPH Agents No compelling evidence to support any changes at this time. Calcium Channel Blockers No compelling evidence to support any changes at this time.
Closed Executive Session	Paul Leary, Medicaid Deputy Administrator	

Pharmacy and Therapeutics Committee
Public Comment
October 19, 2007

J. Anthony Lopez

Hi. Members of the Committee, my name is Dr. J. Antonio Lopez. I am a cardiologist, lipidologist and hypertension specialist in Boise, Idaho. The purpose for me to be here today is to support the inclusion of Coreg-CR in Idaho State Medicaid. As we know, Coreg-CR is a superior beta blocker in heart failure in patients post myocardial infarction with left ventricular systolic dysfunction, as well as diabetes with difficult to control hypertension. Particularly, I'm interested in the support of utilizing this agent in patients with diabetes and with difficult to control hypertension, as we know its mechanism of action is to block all three adrenergic receptors; beta-1, beta-2 and the alpha adrenergic receptor. The studies have demonstrated the benefit of this agent post myocardial infarction, particularly in patients with reduced ejection fractions and reduced mortality in patients with recurrent myocardial infarction, and also in patients on top of an ACE inhibitor who have had myocardial infarctions previously. Also, recent studies have shown its benefit in patients who have diabetes, improving glucose control, less weight gain, as well as lipid parameters, particularly cholesterol and triglyceride. So the importance for me to be here today is to ask for utilization of Coreg-CR in patients with difficult

to control hypertension and particularly because a q.d. formulation will improve patient compliance (interrupted). Patients with high cardiovascular risk are almost always on a large number of medications and compliance is challenging, so a q.d. formulation will make compliance better for our patients in the long term, particularly patients with diabetes, metabolic syndrome, and multiple other cardiovascular risk factors. So, I'm in support of Coreg-CR for management of patients with hypertension.

Heather Cowden, RN

I am calling about the pegylated interferon choices that we have currently and right now I only have the choice of Pegasys with my Medicaid patients. I feel like this is crimping my best practice. I feel that basically I feel more comfortable prescribing Peg-Intron for my genotype 1 patients and over weight patients. Partly because clinically I have personally seen better success with sustained biological response with Peg-Intron. I feel this is in part due to Peg-Intron being weight based dosing and partly due to the kinetics of the molecule. Peg-Intron is less pegylated than the Pegasys which makes it just a bit stronger with the anti-viral and the effects of the medication are experienced more rapidly. So when I am treating these patients the first 12 weeks are the most important and I am seeing effects of this medication in Peg-Intron rapidly rather than with the Pegasys I am seeing it later. I have actually had a patient that I have had to switch mid-therapy from the Pegasys to the Peg-Intron because she was failing. This was prior to your prior authorization rule and she cleared right away. She was a heavy patient, she should have cleared very easily with either medication, but she was heavy and she was older. I just have a lot more faith with Peg-Intron and it's taken me a lot of time trying to get these prior authorizations completed with out the current process. That is basically all I have to say.

Committee question: What is Heather's full name and back ground?

Answer: I am a Nurse Practitioner in Twin Falls, Idaho, that practices in Hepatology and GI.

Tracy Young

Good morning. I'm Tracy Young. I'm a nurse practitioner and I'm also here to discuss Pegasys versus Peg-Intron. I would very much like to have Peg-Intron included on the formulary for Medicaid for our hepatitis-C patients. Before I go any further, I would like to state I'm not under any obligation to either of the companies here. My obligation is strictly to my patients and I'm here speaking on their behalf. Over the years, our clinic has treated a large number of patients with hepatitis-C and in the last three years, I have initiated and managed the majority of that treatment. As with most of the US, here in Idaho, we see more of the genotype 1 hepatitis-C. Many of these, as in the general population, are overweight. Studies have repeatedly demonstrated that patients with certain characteristics do not respond as well to the combination therapy of pegylated interferon and ribavirin. The toughest to treat are those with genotype 1 high viral load and weight over 85 kilograms. Both of the products used currently in treatment naive patients, Peg-Intron and Pegasys, have shown essentially equal efficacy in other genotypes in those patients weighing less than 85 kilograms. Testimony will surely be given here today by both pharmaceutical companies and, as you know, study results can be selectively reported. To my understanding of the literature, ribavirin in combination with Peg-Intron which has weight-based dosing, in effect individualized dosing, appears to have an edge with heavier patients. The makers of Pegasys, which is currently flat dosed,

must also believe this, as they have studied higher doses of their product and seen greater response. Please keep in mind the response I keep referring to is a sustained viral response, a predictor of eradication of hepatitis-C. In those patients who either don't treat or don't respond, there is a significant risk of progression to cirrhosis and developing hepatocellular carcinoma. In these instances, liver transplant is the only remaining option, but at a cost of $300,000 for the transplant and $25,000 yearly for immune suppressant medications. There are presently not enough livers to meet the need, and with the alarming rise in non alcoholic steatohepatitis, the situation promises only to worsen. Obviously, appropriate therapy is the most cost effective avenue, and certainly better for the patients. Avoiding transplant with effective therapy is more humane, cost effective and productive, with active hepatitis-C before a transplant. After the transplant, the hepatitis-C is still present and more aggressive. As I understand it, in order to get authorization for Peg-Intron by Medicaid for my tougher to treat patients, they must first fail Pegasys; forty-eight weeks of side effects, blood draws, and office visits. Then if they fail to respond, ask them to repeat it. There is no evidence that re-treatment with interferon offers much benefit, and even my most motivated patients will be reluctant with no real promise of success. In summary, my goal in treating hepatitis patients is to eradicate the virus. Please allow both medications on your formulary, as there is a place for both, and permit clinicians to make choices of what is most appropriate for each individual patient.

Lynn Lundquist

Good morning. My name is Lynn Lundquist. I'm a urology PA. I work for Don Walker. I'm here to encourage the board to place Detrol-LA back on the formulary. As most of you know, Detrol-LA is the number one overactive bladder medication in the United States. There is no dose adjustment for my patients with multiple co-morbidities, there is no drug interactions, and as far as the safety profile, it is the same as the placebo. One of the biggest things I'm here for is that Dr. Walker and I do see Medicaid patients. A lot of the urologists in town do not, and we are still seeing them, and they deserve to have a choice. There are several other overactive bladder medications out there and they all work, but each individual drug works differently with each person, and so we would like to be given the opportunity to use Detrol-LA back with our Medicaid patients.

Ellen Hunter, MD

I'm from Boise, Idaho and I'm affiliated with Idaho Gastroenterology Association. I'm a gastroenterologist and hepatologist and treat probably the largest number of patients in the state of Idaho with chronic hepatitis-C and I am very familiar with the pegylated interferon and ribavirin treatments. There are two pegylated interferon products, and in my opinion, they work about the same and have similar side effects. I don't have a strong preference for one or the other, but what is helpful in my practice is to be able to have the choice of using one or the other, mainly reducing the side effects that the patient experiences with one pegylated interferon product. If he's having intolerable side effects but having a good response so we can clear the virus, it's helpful to have the option of changing to the other pegylated interferon product, so that we can complete therapy with the hopes of clearing the virus completely so that we're not dealing with cirrhosis and complications of cirrhosis in the future. So my recommendation is to have available both pegylated interferon products in order to make the option of one versus the other if a patient is having intolerable side effects with one or the other.

Committee Question: Doctor, do you find it helpful to use one over the other for your heavier patients because of weight based dosing, or is that not...?

Answer: Um, that is a bit of a concern. I find Pegasys can be helpful in the obese and overweight patients, but I have seen some morbidly obese patients who I thought weren't going to clear it, they have been actually able to clear it with the Peg-Intron products but if I were to choose in an overweight or obese patient, I would probably go with Pegasys for the overweight patients.

Addendum: A second call from Dr. Ellen Hunter occurred, where she corrected a statement she had made in her testimony. The last sentence. "...I would probably go with Pegasys for the overweight patients." should be "...I would probably go with Peg-Intron for the overweight patients."

William Donrad, MD
Of Eagle Rock Neurology of Idaho Falls, Idaho. I am not quite sure what it is that you are looking for. All of these medications, the MS drugs, the Avonex, Betaseron, Rebif, uh, and copaxone should be approved for first-line initial therapy for MS patients. With out preference for any one of them. That reasoning is because some people are going to be able to tolerate one better than another, I think that some people are going to be able to handle medications like glatiramere, and copaxone easier because it is not a foreign protein and the chances of side effects and flu like symptoms are less. On the other hand some people will be able to handle the medications like Avonex, Betaseron and Rebif, just fine with out flu like symptoms or the incidence of neutralizing antibodies. My understanding is these medications all cost about the same amount of money, so I do not think that any particular on should be shown preference, or not shown preference. As a second line in appropriate patients Tysarbi should be covered as well.

William Schmidt
Hi, my name is Bill Schmidt, Penn Pharma Medical Scientist and I would like to thank you for this opportunity to thank the Committee for allowing me to testify on Avodart, which is preferred on the Idaho PDL. Of course, Avodart is indicated for the treatment of symptomatic BPH and it's also being studied in combination with the alpha blockers, as well as for the prevention of prostate cancer. Most of us know that in the prostate, there are two 5-alpha reductase enzymes that convert testosterone into dihydrotestosterone, or DHT, which actually drives prostate growth. Treatment for enlarged prostate can include 5-alpha reductase inhibitors, which inhibit the production of DHT to shrink the prostate, arrest the disease process, and improve urinary symptoms. The two drugs currently available are finasteride and Avodart, and I would like to take a minute or so to differentiate between the two. Avodart does achieve maximal DHT suppression by inhibiting both enzymes, where finasteride only inhibits the type-2 enzyme. In fact, Avodart reduces DHT by about 95% while finasteride reduces it by only about 71%. In a three month prospective of non randomized study to evaluate Avodart and finasteride, there was a significantly greater reduction in symptoms with Avodart, and as noted in Provider Synergy's report, Avodart reduces prostate volume as early as 1-3 months as opposed to finasteride, which produces prostate volume in about 3-6 months. The newest data is from a trial evaluating whether combination therapy of Flomax plus Avodart is more effective than either drug alone. Avodart resulted in significantly improvement in maximum flow rate compared to Flomax from twelve months onward and, as expected, Flomax had no significant effect on prostate volume. We are awaiting further data on the combination on the next study. Avodart has adverse events in controlled studies that were mild to moderate and generally resolved while the patients were on treatment, and in the few trials comparing Avodart to finasteride, there were no significant differences in adverse events between the two groups. In summary, Avodart arrests the disease process, reduces the risk of acute urinary retention and BPH related surgery, and is generally well tolerated. Therefore, I request that the Committee recommend that Avodart remain as preferred on the Idaho PDL and in closing I would say that in future meetings, I look forward very much to presenting more new data on Avodart, particularly from the ongoing trials involving prostate cancer. Thank you.

Don Moran

Good morning, I'm Dr. Donald Moran, a member of the Department of Medical Affairs at Sanofi Aventis. My colleagues at the company and at UCB Pharmaceutical want to draw your attention to a new, third generation antihistamine approved by the FDA in May of 2007. This product is approved for the clinical manifestations of both seasonal and perennial allergic rhinitis, as well as the skin manifestations of chronic idiopathic urticaria. Now, I say it's a third generation product as such; it's an improvement on technology. Its parent compound, cetirazine, has been technologically modified. Xyzal brand levocetirazine is the R-enantiomer from that mixture. As such, it has pharmacokinetic and pharmacodynamic properties that are consistent with lower blood-brain penetration, more consistent and more significant impact on wheal suppression as demonstrated through skin prick histamine tests in patients pretreated with levocetirazine versus comparators, such as loratadine, desloratadine and several other European antihistamine products. It's also a product which had a greater affinity and receptor occupancy than other antihistamines. Translating this into clinical practice, what does this mean? Well, it's a product that essentially has a faster onset of action and longer duration of action than its comparator desloratadine and placebo. It's a substance also with more significant improvement in nasal air flow and congestion as demonstrated subjectively and by nasal turbinometry than desloratadine and placebo, and is also with a faster onset and more sustaining symptom complex activity reduction than the leukotriene receptor antagonist, Montelukast. It's proven in adults and children age six and above, it's a product which has an absolute somnolence rate of 6% approximately versus a 2% absolute rate of somnolence in patients on placebo. This is actually less than its parent compound, cetirizine as a somnolent side effect. No clinically meaningful effect on QT/QTc interval prolongation, it's a pregnancy category-B product, and it's a product that's also unlikely to produce any kind of pharmacokinetic interaction with other products. At a time when allergic disease continues to be the fifth most prevalent condition in the United States per the CBC, at a time when two-thirds of patients report that they are still not satisfied entirely with the allergic products available to them, at a time when only 45% of physicians are entirely happy with products, I think it's a very reasonable, logical option to offer patients and members of the State of Idaho. I urge you to look at it seriously and consider it for inclusion on the PDL. Can I address any comments, thoughts or questions? All right, thank you.

Christopher Spell

I want to thank the members of the Committee this morning for allowing me the opportunity to come and present. My name is Dr. Christopher Spell and I represent the Medical Affairs Department of Sanofi Aventis. This morning, I am speaking on behalf of Uroxatral for treatment of benign prostatic hyperplasia. As an alpha-1 adrenoreceptor antagonist, the drug has had a phenomenal track record of use in both Europe and also in the United States. History of safety and efficacy: three clinical trials which led to the confirmation of the drug for approval in 2003 by the FDA have shown significant improvements in BPH symptoms, such as with irritative and obstructive symptoms, as well as benefits on nocturia and even sexual function. The onset of action of the agent has been seen as early as eight hours after the first dose, and at full twenty-four hour coverage, due to the fact that the drug is a 10 mg sustained-release pill. This effect has also been noted regardless of prostate size, but also in terms of acute urinary retention, there have been benefits noted as well, in terms of normal voiding after an episode and also in reduction of the incidents of episodes occurring after that. In terms of safety, the most common or most prevalent side effect of Uroxatral has been dizziness. However, also concerns about vasodilatory effects have been noted in several clinical studies. In combination with antihypertensives regardless of age and co-morbidities, the drug has shown a fairly low incidence in differences in mean blood pressure, as well as heart rate. In addition to that, a combination of PD5s, literature reports have shown that the combination of tadalafil and sildenafil, that the drug has not resulted in significant clinical or hypotensive effects. Finally, one of the other aspects to differentiate some from the class has been in terms of sexual function. There have been factors related to comparison potentialism in other agents in the class. What has been noted is that the drug has had very low and

insignificant differences in sexual function or premature ejaculation in male subjects. I would like to thank you again for this time and also ask for the continued consideration of Uroxatral for the state formulary.

Kyle Downy

Good morning Committee members. My name is Kyle Downy, I'm a Regional Medical Liaison in Cardiovascular for Sanofi Aventis, there are three of us in a row this morning. I'd like to thank you for your time and hearing my testimony on inject able anticoagulants. Lovenox is the most widely used and published and widely low-molecular-weight heparin anti-10A agent, and has the most FDA approved indications within the class. To date, over 100 million patients have been treated with Lovenox in ninety-six countries and it has indications encompassing both prophylaxis and treatment of venous thromboembolism, as well as acute coronary syndromes. Lovenox has been recently approved for the STEMI indication of ST-segment elevation MI and is now indicated across the ACS spectrum. As well as Lovenox is the only low-molecular-weight heparin that has been proven safe and effective for outpatient use and post hip replacement surgery, as well as outpatient treatment of DVT, providing pharmaco-economic advantages for transition from an inpatient to an outpatient basis with the Medicaid program. Universal organizations including the FDA have physician statements to indicate that the low-molecular-weight heparins are not interchangeable. Additionally, there is positive data of well done, head-to-head trials and, therefore, every low-molecular-weight heparin should be considered of its efficacy based upon individual indications for each patient. Lovenox has an excellent risk/benefit profile and numerous pharmaco-economic analyses evaluating it that have demonstrated either cost neutrality, as well as cost savings, especially when looked at transitions to outpatient basis for treatment of DVT. It is also the only low-molecular-weight heparin agent that has an FDA approved indication for dosage adjustments for severe renal dysfunction and has data for the use in the pediatric and pregnant patient populations. Nationally, greater than 90% of patients receive Lovenox as a low-molecular-weight heparin, indicating a strong comfort amongst providers, physicians, as well as health care providers. So in conclusion, Lovenox is a cost effective inject able anticoagulant with extensive trial and practice experience through wide indications and further treatment. It has simple dosing strategies which minimizes health care professional time and enhances patient compliance. Finally, for the treatment of DVT, the ability to transition patients to the outpatient setting is cost effective for the health care system, and I would request that Lovenox be maintained as the preferred agent on the State of Idaho formulary. Thank you and if I can answer any questions?

Molly Roy, PA

Good morning. My name is Molly Roy and I'm a physician's assistant. I recently returned to Idaho after practicing in Salt Lake City for two years. I practiced with Dr. John Foley at the Rocky Mountain MS Clinic, where we had nearly 1,500 MS patients. I am here this morning on my own account to share with you experiences I have had in treating hundreds of MS patients in hopes that you will allow all six of the major MS medications, including Avonex, Rebif, Betaseron, propaxone, mitoxantrone and natalizumab to remain on the Idaho formulary to help the Medicaid patients of Idaho. There are a few different factors we take into consideration when choosing MS medications for our patients, and I think it's important to keep in mind that, like a lot of diseases, MS is very different in each patient and although some of the medications have similar or the same mechanisms of actions, they don't always work similarly in each MS patient. I've seen, on numerous occasions, patients who have not responded to MS medications with a certain mechanism of action, and then switched to another medication of a similar or even the same mechanism of action, and had dramatic response, so I think it's important that although some medications are similar in their mechanism of action, they all remain on the formulary. Side effects and tolerability are the big issue with MS medications because they can have pretty severe side effects and can limit the patient's ability to work or function, and it's important for the patient to be able to switch between the medications if they are unable to tolerate each or one of the medications, so that they can find something that they respond with, and lastly compliance is a huge issue with these medications. As you may or may not know, all of the medications involve needles; they are not oral medications, so it's difficult for

patients to be complaint and the medication frequency ranges from daily injections to multiple times a week to once a week, up to once a month and every three month infusions, so if the patient is on a medication that they are not going to take compliantly, they are not going to get a response, and that's why it's important to allow them to have the option of choosing a medication that they will take compliantly and have type of response. So those are the three things that I take into consideration when talking with the patient so that we can choose a medication that is most appropriate for them that they will find a good response with. Thank you very much. Any questions?

Committee question: In your practice, where do you use Tysabri.

Answer: What type of patient?

Committee response: Uh huh.

Answer: So, of course the FDA has mandated that it's not a first line therapy, so we didn't use it first line. They had to fail one of the other therapies first, and by that we mean either didn't have a good response or were not able to tolerate either because of liver toxicity or just even flu-like symptoms that were so severe that the patient couldn't function or go to work or anything else, then we considered them, but of course there was a huge consent process with all the risk factors that were involved with that. Any others? Thank you.

Rosalynde Finch

Thank you, Dr. Rosalynde Finch, Biogen Idec, the makers of Avonex and Tysabri, so good timing, following after Molly Roy, and actually I was going to say some of the same things she said; I'm not going to repeat them about how MS is different in every patient and patients' reactions to the drugs. I am here to advocate the open and equal access to all the medications as well, really this a treatment decision that needs to be made at the clinical level between the physician and taking into consideration the needs of the patient. So, with that being said, I would like to, for you to appreciate the strengths of our MS products and why they should continue to be available to all patients with MS. So, Avonex is the only MS treatment with FDA approval on the labeling for all three key areas, and that is reduction in disability progression, reduction in relapse rate, and decrease of adverse attack. The AAMMS Counsel has issued its statement that the most important therapeutic aim of any MS therapy or any disease modifying treatment of MS is to prevent or postpone disability progression, and we agree completely with that statement and I would say that I would add most patients, that's their primary concern, is disability progression. So in support of that aim, Avonex is the only self inject able agent that has prevention of disability progression as the primary end-point in their pivotal trial, and it's the only disease-modifying treatment with class-1 evidence demonstrating a 37% halt or reduction in disability progression, and that sustained over the six month time point, which is the most stringent criteria. Also, data for all these agents was limited to just two or three year studies, and that's before the effect of neutralizing antibodies can be seen. That's pretty critical, because if a patient develops neutralizing antibodies, the interferons are no longer effective for them, so Avonex is the least immunogenic of the interferons. I'm also here to say that drugs don't work of they're not taken. You all know that. Avonex has a very high compliance rate, it's a once-a-week injection, 75% of patients are still on Avonex after eight years; that's incredible compliance for a self inject able. Then, lastly, patients with a chronic and disabling disease like MS should not be forced to switch to another therapy if they are compliant and stable on their medication. If you have to switch to something like a three times per week injection or a daily injection, then that is going to risk compliance. So, I'm also here to advocate for open access to Tysabri. It is the most efficacious MS treatment available. I do need to correct what Molly said, the FDA did not mandate that it couldn't be used as first-line therapy, that it is open to the discretion of the physician.

Long Nguyen
Thank you very much, my name is Long Nguyen, I represent SmithKlineBeacham on Coreg CR. The OHSU beta blocker final report reviewed Coreg CR and had said that carvedilol has the strongest evidence of reducing mortality from heart failure and post MI and that there are no differences seen in terms of carvedilol and Coreg-CR. That is true, because based on bioequivalency data at the equivalent dose, Coreg-CR provides the same plasma drug concentration as those taking carvedilol twice a day. However, the OHSU report does not address the effect of compliance or adherence in term of outcomes, and there's a trial called a BHAT trial, which is the beta blocker heart attack trial, that demonstrates or shows that patients who take less than 75% of their beta blocker are 2.6 times more likely to die within the first year of follow-up after their heart attack, and if you think about carvedilol which scientifically has been shown to be the best in mortality reduction among this class, and if the patient is taking carvedilol twice a day and if they miss one dose, the compliance rate has already dropped to 50%, which would significantly puts them at risk for any type of cardiovascular event. In addition to that, we have very few data to support the fact that improvement in adherence or compliance leads to improved outcomes. There was an observational study that looked at 4,700 patients with heart failure and post MI that showed that increase in 10% of adherence and compliance in medications result in a 9% risk reduction in cardiovascular hospitalizations which can translate to at least a 6% reduction in health care costs. So, we all know that it doesn't matter how good the drug is if the patients have an issue taking or missing the drug; they are not going to be able to benefit from it. So, with Coreg-CR availability, not only do you have the drug that is the best in its class, but we have an ability to make the drug accessible to the patients, because unless the patients have access to the drug to be able to benefit from it, then they would not be able to benefit from the drug that the doctors prescribe. So, I'm here to ask the Committee members to consider making Coreg-CR accessible to your patients, so that not only could they get benefit from the drug itself, but simplify their drug regimen daily, especially if these patients are taking multiple medications multiple times a day for multiple disease states. With that, thank you very much for your time and I would be happy to answer your questions.

Heather Potter
Hi, I'm Heather Potter, I'm here on behalf of the National Multiple Sclerosis Society. I just wanted to come and thank you for the opportunity to share what our National Clinical Advisory Board recommends with the six FDA approved medications. Briefly, they would like to continue to have open access to all medications. They all have been found beneficial, and as Molly was saying, they all reduce relapse rates and improve the quality of life of those with MS. Based on their tolerability, we would like to see each medication continued. I work with over 1,800 people with MS in Idaho and they would like to have the opportunity with their physician to choose which medication, which type of injection, and which side effects they would like to have. Any questions?

Fred Amberger
Good morning and thank you for your time. I'm Fred Amberger. I'm a Regional Scientific Director with Novartis Pharmaceuticals, I'm in the Medical Affairs Department. I would like to offer essentially three points for considering Enablex to be retained on the Idaho PDL. The first is that in electrophysiology studies, Enablex was studied at doses of 15-75 mg. 75 mg is five times the maximum recommended dose. In this study, there was no change in QT signals that was seen with the drug. Additionally, anticholinergic drugs have been associated with increases in heart rate and in tachycardia. In the phase II and phase III trials that were done with Enablex, there was no change in heart rate relative to placebo. The second reason for considering Enablex is CNS effects. With anticholinergics, it's not uncommon to see memory deficits with disorders, confusion and hallucinations. Enablex has been studied in a three-week, double blind, placebo controlled trial that showed that there was no difference in memory recall compared to placebo. And lastly, Enablex has demonstrated long-term bladder control. It's the only OAV drug to have long-term

opened label data published to date. In the two-year study that was published, it was reported that the efficacy of Enablex was increased by 63% at twelve weeks to 84% at two years, with no increase in adverse events. Discontinuation due to constipation and dry mouth were comparable to the twelve week studies. Thank you very much. Are there any questions that I can answer? Thank you.

Sylvia Foster

Good morning, I'm Sylvia Foster, I'm a pharmacist and a medical scientist for GlaxoSmithKline. I'm here to discuss Arixtra or fondaparinux for the inject able anticoagulation class. Currently on formulary, there are three agents, Lovenox, Fragmin and Arixtra. Lovenox and Fragmin are low-molecular-weight heparins, they are in the heparin class. Arixtra is the only non-heparin injectable anticoagulant currently available. It's the first of many that are on their way to the product marketplace. It's synthetic. It's not pork derived, and for that reason it's important to have it on formulary for those patients who have an allergy to heparin or a history of heparin-induced thrombocytopenia. I have worked as a hospital pharmacist for ten years and in an outpatient anticoagulation clinic for two years, and I have used all of these agents. Why would I choose Arixtra for my patients as opposed to the others? I think there's a place for all three of these agents, but you need Arixtra because, first of all, it's a non-heparin and synthetic, it has a very predictable dose response, the dose is very simple; 2.5 mg once a day for prevention of blood clots, 5 mg, 7.5 mg or 10 mg once a day for the treatment of blood clots, and that depends on what weight group you're in. The important thing is that it's once a day. For outpatient treatment of DVT or PE, Lovenox is a twice-a-day drug and Arixtra is once a day, and that's important for compliance. In the clinical trials for prevention of VTE, it shows better efficacy versus Lovenox in the prevention of VTE in orthopedic surgery, as far as the treatment of VTE, equal safety and equal efficacy compared to Lovenox, and another thing to point out for cost purposes is that with Lovenox, the more milligrams you need to use, the more it costs, and you have to calculate the dose; 1 mg/kg q 12 hours. So for those heavier patients, it tends to cost more. With Arixtra, it's the same cost, whatever the patient weighs, so as you get to the heavier patients, you see a cost benefit there. Lovenox has been around for over fifteen years, it's definitely the.... (tape ended).

Leigh Platty

Good morning, my name is Leigh Platty and I'm the scientiific liaison for Astellas and I'm here today to talk about solifenacin VESIcare for overactive bladder. The goal of therapy in treating overactive bladder is to keep the patient dry, with the minimum side effects. In the registration trials of over 1,800 patients, 51% of the patients were dry at the 5 mg dose, there was less than 11% rate of dry mouth. In the long-term registration trials, there was good evidence of high persistence, with 81% of the patients still on the drug at the end of one calendar year. Half life is about fifty hours, so yet the study stated about ten days, it gives you good, even blood rates over twenty-four hours. In the STAR trial, solifenacin 5 mg and 10 mg were compared to tolterodine 4 mg long-acting. 49% of the patients on tolterodine were dry and 59% of the patients on the solifenacin. The secondary end point has tended to favor solifenacin, as well as did the patient's perception of their own bladder condition. With the VENUS trial, the primary end point was urgency and solifenacin was significantly superior to placebo in reducing episodes of urgency and urge incontinence with increasing warning time. Now urgency was chosen as the primary end point because the Internal Continence Society stated that urgency was the driving symptom of the overactive bladder complex. In inpatient focus groups, patients related to us that urgency was a great concern and was very bothersome because it affected their quality of life. There was that fear of having a wetting accident in public, and that curtailed their activities and their social life. We also did warning time. A warning time was measured by a stopwatch. The patient's were told to start it when they felt that strong desire to void and to stop when they actually voided. The difference was 32 seconds. There was 32 seconds more time to try to find a bathroom. So in conclusion, in every clinical trial, at least half the patient's were dry, there was reasonable side effect profile, and they had some additional time to try to find a bathroom. Thank you very much. Are there any questions? Thank you, I appreciate your attention.

Gina Guinasso
Good morning, my name is Gina Guinasso and I'm an account manager with EMD Serono. Unfortunately, the medical science liaison that had planned to present could not make it this morning, so I'm going to provide his comments in support of Rebif inclusion on the PDL. In 2002, the American Academy of Neurology published the article "Disease modifying therapies in MS". The article defines three key efficacy parameters of MS trials. Number one, a reduction in relapse rates, number two, delaying progression of disability, number three, T2 volume change on MRI. When looking at these end points, in each one of the drugs pivotal trials, only Rebif had a statistically significant effect on all three key efficacy parameters. When Rebif was approved outside of the United States in 1998, it was not allowed to enter the US marketplace because Avonex held the orphan drug status. To gain entrance into the marketplace, Serono undertook the EVIDENCE trial, the only published class-1 head-to-head trial of DMDs. Based on the result of the EVIDENCE trial, Rebif was allowed to overturn the orphan drug protection that Avonex held, and Rebif entered the US market in 2002. It was the first time in the over twenty-year history of the Orphan Drug Act that the Act was overturned based on clinical superiority as defined by the FDA. Additionally in the EVIDENCE trial, the side effects, the severe adverse events, and drug discontinuations were comparable between Rebif and Avonex. Next, I would like to highlight the information regarding Rebif and Betaseron as noted in the DERP report. In an effort to compare the efficacy of Rebif and Betaseron, DERP reviewed two small studies, neither of which found a significant difference in efficacy, however the DERP report states both on Table 2, pg. 16 and Table 5, pg. 21, "Rebif had superior tolerability, as measured by fewer injection site reactions, fewer flu-like syndromes, and less depression when compared to Betaseron". We hope that Rebif will continue to be made available to patients in Idaho. Thank you for your time.

Robert Martin
Members of the Committee, my name is Robert Martin and I'm a PharmD and a member of the medical science team with Bayer Healthcare Pharmaceuticals. I'm here to testify on behalf of Betaseron's inclusion in the Idaho PDL. Betaseron or interferon beta-1b is indicated for the treatment of relapsing forms of multiple sclerosis and to reduce the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been established to include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis. This new indication is based on results from the BENEFIT study. In this study, patients with a first clinical demyelinating event and MRI features suggestive of MS, Betaseron is the only high-dose, high-frequency interferon beta that is FDA approved for use in the earliest stages of MS. In benefit, Betaseron significantly delayed progression from the first single clinical demyelinating event to the time when there was evidence of clinically definite multiple sclerosis. The proportion-hazards regression analysis showed a 50% reduction in the risk of progression to clinically significant multiple sclerosis. A three-year integrated analysis of the data from BENEFIT and its open label extension which was published recently in The Lancet confirmed a sustained and statistically significant effect of early Betaseron treatment in reducing the risk of progression to clinically definite MS. Furthermore, immediate treatment with Betaseron resulted in a 40% reduction in the risk of sustained disability progression measured by EDSS as compared to delayed treatment. Betaseron is the only drug proven to delay disability when used at the earliest stage of MS or the first demyelinating event, also referred to as Clinically Isolated Syndromes. To date, Betaseron has the longest evaluation period of clinical efficacy of any interferon beta in multiple sclerosis. Time up? Thank you. Any questions?

Sue Heineman
Good morning. I'm Sue Heineman, I'm a pharmacist here in Boise and a Medical Outcome Specialist with Pfizer, here to talk about Detrol-LA or tolterodine extended-release. This is the only agent in this category that is non preferred. As I mentioned last year, I think it was in May of 2005 that you guys declared this as a preferred agent, last year became the only non preferred. It has the most extensive clinical database showing

safety and showing efficacy. It was the #1 prescribed agent with Medicaid patients, it is currently at 5% utilization, so it's still being used. There is still a place for it. When you look at your own CMS available data, the cost, and this doesn't include your rebates, which are not available, but even the cost per prescription is less than oxybutynin-XL, garafenicin, and solifenicin, so the cost is cheaper, and there isn't any other agent that has shown superiority in primary efficacy end points. There was a mention earlier of the STAR trial, which is a non inferiority trial, so no claim to superiority should be made, it has shown safety in elderly patients, it has shown safety in male patients when, of course, you think it's a prostate issue when men have actually bladder control problems and putting them on tolterodine-ER, there were no problems with some of the side effects that you would expect; there aren't those anticholinergic side effects that you see. So I just would respectfully request that you reconsider adding tolterodine-ER back to the preferred drug list. Thank you.

Vandanna Slater

Good morning. My name is Vandanna Slater, the Medical Liaison for Roche Urology and a pharmacist by training, here to testify on Pegasys. The CDC estimates 3.2 million Americans are chronically infected with hepatitis-C and it is currently the leading indication for liver transplant. With FDA approval in 2002, Pegasys with ribavirin has become the most prescribed treatment for patients infected with chronic hepatitis-C for five main reasons: first, Pegasys with ribavirin has the broadest range of FDA indications, including the following unique to Pegasys. In patients with compensated cirrhosis, for chronic hepatitis-C infected patients with currently stable HIV disease, and as monotherapy in patients with chronic hepatitis-B. Second, a wealth of clinical data supports the Pegasys label and has set new treatment standards, such as combination therapy with ribavirin 800 mg for a shorter duration of 24 weeks with genotype-2 and -3 patients. Eight key studies with Pegasys and hepatitis, the most recent this summer, have been published in the New England Journal of Medicine. Third, Pegasys offers durability of response. Rate is at 99% of patients who achieve an SBR following Pegasys alone or with ribavirin remained HCV-RNA-negative for a minimum of 4.1 years. Fourth, Pegasys is easy to use. It's administered as one standard dose, it is not dosed by weight. It has a unique pegylation profile that allows for smaller volume of distribution, so it's one standard dose given as a ready-to-use, prefilled syringe except for with dialysis patients, and it is important to note that at greater than 85 kg or 187 lbs, both pegylated interferons were given as a fixed dose, 150 µg for Peg-Intron and 180 µg for Pegasys. Fifth, Roche's commitment to optimized therapy for HCV includes research to improve response rates and a strong pipeline. Pegasys has a comprehensive support program available 24/7 to help patients and providers to help manage hepatitis therapy. So overall, for broadest range of FDA approved indications, ease of use, a wealth of clinical data and experience with Pegasys, we believe offers hepatitis-C virus patients and chronic hepatitis-C patients, including the most difficult to treat, the best chance for treatment outcome. Thank you.

Katrina Kuznetsova

Thank you very much for the opportunity to present here on behalf of Peg-Intron and, well I am physician and I represent Schering-Plough. I am in Research & Development part of the company. That means that my salary, bonuses or any compensation will be not affected, directly at least, affected by the results of this meeting. So, there are only two pegylated interferons on the market right now available. They are packaged and they are dose differently, and I do believe that they both should be available for patients. So I can give you a quick, five good reasons to place Peg-Intron on formulary and make it available for patients, but I would be preaching to the choir today with healthcare professionals, and tell you that Peg-Intron is an individualized based product that has an advantage over peg-alpha-2a in patients over 85 kg. So Pegasys is given as a fixed dose for all patients' weights and Table 17 in the FDA briefing clearly states when the patient gets heavier, they sustained response rate is dropping with peg-alpha-2a. That doesn't necessarily happen with Peg-Intron. As patients get heavier, it's more difficult to treat patients, yes that's right, but the sustained response rate is, regardless of weight category, is pretty much similar and I am quoting right now two large trials. One is WIN-R, which is 5,000 patient database, and another one is (sounded like POWER), which presents the final results at AASLD this year.

So Pegasys is doing post approval commitment studies with the higher doses of Pegasys in patients over 180 lbs and I can tell you that the results of these abstract studies have already been presented and frankly, each and every one of the studies demonstrate that it is a higher response when you individualize the dose of the drug. So, I know you will be reviewing later on the Oregon Health Science University report. Well, that report is very comprehensive document. However in the report, they didn't look at the patient weight as a predictor of response rate. They have only "obesity" there and, you know, let's look around the room here. If you ask any male here to stand up, probably each and every male over 180 lbs will be up right now, almost each and every male here over 180 lbs, but they are not obese. So the point I'm trying to make: weight is a predictor of sustained response rate when you're not individualizing both products, PEG and ribavirin. Well, as the report also mentioned, there is no sufficient head-to-head data right now, but ideal study will be presented at the spring next year. This is five, oh, I'm sorry, three thousand patients data base comparing Peg-Intron to Pegasys, but please don't wait for this study to come along. Please add ribavirin in formulary or make it somehow available for patients because as a clinician, you need to pick and choose. Only two drugs available, difficult it is to treat forty-eight weeks of treatment. Please make it available for patients. Thank you very much for your time. Any questions for me? No? Thank you.

Jack Kreiger

My name is Jack Kreiger, I live here in Boise, Idaho, I'm a member of the Boise Hepatitis-C Support Group, and a consumer of this product. I have had treatment for hepatitis-C. I believe that the treatment should be between the provider and the patient and that there's only two brands and that they should make the decision. For you guys that fish, you'd hate to go out on the stream with only one fly; it wouldn't be very productive, so that's the same kind of thing I'm thinking. The support group that I belong to has old and young people, short and tall, underweight, overweight, responders, non responders, liver transplants, and folks who are not ready to try the treatment. And those who have had treatment and still come to the meetings share their experience, strength and hope with each other, and being a past treatment person, I know that all side effects are different, depending on the people. That's the stuff we talk about, so I would like them to have the opportunity to decide what type of treatment they would like. Then there are the providers who come and share their experience with us and let us know about the disease. I've gotten more information in the support group than I have any other place, and I'm here just as a consumer, and I just want us to have the choice. The people. When I had prostate cancer, I had a choice of what kind of treatment I wanted. We discussed it with the provider and I took the best option I thought would work for me. That's all I want for the people who need treatment. Thanks for allowing me to be here.